

mammal is cloned by nuclear transfer from a quiescent cell obtained from the individual non-human mammal.

52. (NEW) The non-human mammal of claim 51, wherein the non-human mammal is selected from the group consisting of cows, sheep, pigs, goats, mice, and rabbits.

53. (NEW) The non-human mammal of claim 51, wherein the cell is a cultured cell or the cell is genetically modified.

54. (NEW) The non-human mammalian embryo of claim 51, wherein the cell is a cell in which quiescence has been induced.

55. (NEW) The non-human mammalian embryo of claim 51, wherein the cell is a cell that is naturally quiescent. -

REMARKS

Reconsideration of this application is respectfully requested.

Claims 20-42 have been amended. In accordance with 37 C.F.R. §1.121(c), a marked up version of the claims showing the changes from the last version is attached. Claims 43-55 are new and are derived from claims 20-42.

Claims 20-55 are fully supported throughout the specification. For example, applicants' specification supports the recitation of embryos and mammals that have the same set of chromosomes as an individual non-human mammal. Since the nucleus used for nuclear transfer comes from a single individual, the resultant progeny and the progenitor individual have the same set of chromosomes. The specification describes that nuclear transfer allows the production of genetically identical individuals.

(Specification at 1, lines 6-20.) The specification indicates that the invention is useful as a means for cloning animals, and that adult cells can be used for nuclear transfer. (*Id.* at 5, lines 10-24, and at 7, lines 13-33.) The specification indicates that animals produced by nuclear transfer from a source of genetically identical cells share the same nucleus, but may differ in their oocyte contribution. (*Id.* at 19 lines 6-27.) The oocyte chromosomes are removed prior to nuclear transfer. (*Id.* at 26 lines 6-27.) Cells that are obtained from an individual mammal may be grown in culture or modified after being obtained prior to use in the nuclear transfer process (*Id.* at 1 lines 22-33). In an example in the specification, cell lines were karyotyped prior to nuclear transfer and showed a complete $2n$ set of chromosomes. (*Id.* at 32-33). An epithelial cell line obtained by culturing cells from an adult sheep was used to clone a sheep by nuclear transfer. (*Id.* at 32-34.) This sheep had the same set of chromosomes as the individual sheep from which the cell donor nucleus was obtained.

The use of quiescent cells obtained from an individual non-human mammal, thereby producing a clone that has the same set of chromosomes as the existing individual, provides considerable advantages over other cloning methods. For example, the phenotypic characteristics of a number of individuals can be assessed and those with the most favorable traits can be selected for cloning using the claimed methods. The selection of favorable agricultural traits, such as milk yield in dairy cows, often requires that the individuals being assessed be grown to sexual maturity prior to the selection procedure. In contrast, methods that rely on the use of embryonic donor cells (see, for example, U.S. Patent 5,057,420 cited by the Examiner in the March 1, 2000, Office action) do not permit the assessment of phenotypic traits of an individual animal

prior to cloning, nor do they result in the production of embryos or mammals that have the same set of chromosomes as a selected individual non-human mammal.

New claims 43 and 47 specify that the embryo is, or can be, a cow embryo, and new claims 44, 45 and 52 specify that the non-human mammal is, or can be, a cow. Support for the use of the invention to clone various animals, including "cattle" and a "cow or bull," is found in the specification at page 5, lines 10-24 and in the claims as filed. Applicants have employed the term "cow" for grammatical simplicity, and intend this term to cover both male and female bovines. A copy of the relevant entry from The American Heritage Dictionary of the English Language (Third Edition) is enclosed herewith in support of this usage. Should the Examiner be concerned with this usage, applicants will amend the claims accordingly.

No new matter is introduced by this amendment. Upon entry of this amendment, claims 20-55 are pending in this application.

Double Patenting Rejection

Claims 20-42 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,147,276.

Applicants will provide a terminal disclaimer when the claims in the present application are indicated to be otherwise allowable.

Rejections under 35 U.S.C. § 102(b)/103(a)

The pending claims were variously rejected over several publications that teach the production of transgenic animals (Simons et al., 1988; Verlander et al., 1993; Ebert et al., 1991; Meade et al., 1990; and Massoud et al., 1991). However, in each case, the cited art teaches conventional means for producing transgenic animals, e.g., injection of vector DNA into the pronucleus of cells of the early embryo. The resultant animals/embryos are transgenic (although chimaeric), but they are otherwise the products of conventional reproduction in that they arise from the combination of male and female gametes. That is, the animals taught by these references do not have the same set of chromosomes as either one of their parents, but are genetic composites, containing chromosomes from each parent.

In contrast, as described above, the non-human embryos and mammals addressed by the claims of this present application have the same set of chromosomes as a single individual progenitor, in that they are produced by nuclear transfer using a nucleus from a cell obtained from a single pre-existing individual mammal.. Thus, the cited references do not anticipate the claimed subject matter. Furthermore, not one of the cited references teaches or suggests the use of quiescent cells and nuclear transfer to produce embryos and mammals that have the same set of chromosomes.

Accordingly, withdrawal of these rejections is respectfully requested.

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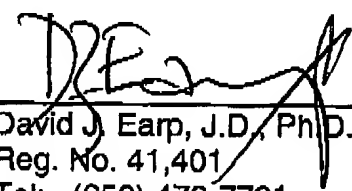
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Applicants respectfully submit that this application is now in condition for allowance. If the Examiner believes that issues remain to be addressed before a Notice of Allowance, applicants respectfully request an Interview with the Examiner prior to issuance of an Action.

Respectfully submitted,

Dated: November 27, 2001

By: _____


David J. Earp, J.D., Ph.D.
Reg. No. 41,401
Tel: (650) 473-7721
Fax: (650) 473-8654

MARKED-UP VERSION OF CLAIMS 20, 29, AND 35 SHOWING CHANGES MADE

20. (AMENDED) A reconstituted non-human mammalian embryo that has the same set of chromosomes as an individual non-human mammal, wherein the embryo is made by a process comprising:

(a) transferring the nucleus of a quiescent diploid donor cell of [a first] an individual non-human mammal into a suitable enucleated recipient cell of a [second] non-human mammal of the same species, thereby obtaining a reconstituted cell;

(b) activating the [reconstituted] recipient cell before, during or after nuclear transfer; and

(c) incubating the reconstituted cell such that an embryo develops that is capable of developing to term and has the same set of chromosomes as the individual non-human mammal

[, wherein the mammalian embryo is of a species selected from the group consisting of: sheep, pigs, goats, mice and rabbits].

29. (AMENDED) A non-human mammal that has the same set of chromosomes as an individual non-human mamma, wherein the mammal is produced by a process comprising:

(a) transferring an embryo according to claim 20 to a female of the same species; and

(b) developing the embryo into [the] a non-human mammal.

35. (AMENDED) A non-human mammal that has the same set of chromosomes as an individual non-human mammal, wherein the mammal is prepared by a process comprising:

- (a) transferring the nucleus of a quiescent diploid donor cell of [a first] an individual non-human mammal into an enucleated oocyte of a [second] non-human mammal of the same species, thereby obtaining a reconstituted cell;
 - (b) activating the [reconstituted cell] oocyte before, during or after nuclear transfer;
 - (c) incubating the reconstituted cell such that an embryo develops;
 - (d) transferring the embryo to a female of the same species; and
 - (e) developing the embryo into [the] a non-human mammal that has the same set of chromosomes as an individual non-human mammal
- [, wherein the non-human mammal is selected from the group consisting of sheep, pigs, goats, mice and rabbits.

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covington (kōv'ing-tan). A city of extreme northern Kentucky on the Ohio River opposite Cincinnati. Settled in 1812 on the site of an earlier tavern and ferry landing, it is now heavily industrialized. Population, 49,563.

cow (kou) *n.* 1. The mature female of cattle of the genus *Bos*. 2. The mature female of other large animals, such as whales, elephants, or moose. 3. A domesticated bovine of either sex or any age. — *Idiom*. *fill the cows come home*, *informal*. For a long time; indefinitely: *The guests stayed till the cows come home*. [Middle English *cow*, from Old English *cū*. See *g^ou-* in Appendix.] — *cow* *adj.*

cow (kou) *tr.v.* **cowed**, **cow-ing**, **cows**. To frighten with threats or a show of force. See Synonyms at *intimidate*. [Probably of Scandinavian origin.] — **cow-ed** *adj.* (-id-lē) *adj.*

coward (kou'ard) *n.* One who shows ignoble fear in the face of danger or pain. [Middle English, from Old French *coward*, from *caud*, *tail*, from Latin *cauda*.] — **cow-ard** *adj.*

coward (kou'ard), Sir Noel Pierce. 1899–1973. British actor, playwright, and composer especially noted for his witty and saddy comedies, such as *Hay Fever* (1923) and *Private Lives* (1930).

cowardice (kou'ard-is) *n.* Ignoble fear in the face of danger or pain. [Middle English *cowardise*, from Old French *cowardise*, alteration of *coward*, from *coward*, *coward*. See *coward*.]

cowardly (kou'ard-lē) *adj.* Exhibiting the characteristics of a coward, particularly ignoble fear: *a cowardly surrender*. — **cow-ard-li-ness** *n.* — **cow'ard-ly** *adv.*

cowbane (kou'bān') *n.* 1. A perennial North American herb (*Oxypolis rigidior*) having pinnately compound leaves and umbels of small white flowers. 2. Any of several related plants, such as the water hemlock.

cowbell (kou'bēl') *n.* A bell hung from a collar around a cow's neck.

cowberry (kou'bēr-ē) *n.* 1. A low, creeping, evergreen shrub (*Vaccinium vitis-idaea*), native to northern parts of North America and Eurasia and having drooping clusters of small white or pinkish flowers. 2. The edible red berry of this plant, used to make sauces, jams, and preserves. Also called *lingberry*, *lingonberry*, *mountain cranberry*.

cowbird (kou'būrd') *n.* Any of various blackbirds of the genus *Molothrus*, especially the common North American species *M. ater*, that lay their eggs in the nests of other birds and are often seen accompanying herds of grazing cattle. [From their habit of staying with cattle.]

cowboy (kou'boi') *n.* 1. A hired man, especially in the western United States, who tends cattle and performs many of his duties on horseback. Also called *♦ buckaroo*, *♦ cowman*, *♦ cowpoke*, *♦ cowpuncher*, *♦ vaquero*, *♦ waddy*. See Regional Note at *vaquero*. 2. An adventurous hero. 3. *Slang*. A reckless person, such as a driver, pilot, or manager, who ignores potential risks.

cowboy boot *n.* A high-arched boot with a high Cuban heel and usually ornamental stitching.

cowboy hat *n.* A felt hat having a tall crown and very wide brim. Also called *ten-gallon hat*.

cowcatcher (kou'katch'er, -ketch'-) *n.* The metal grille or frame projecting from the front of a locomotive and serving to clear the track of obstructions.

cow college *n.* *Informal*. 1. An agricultural college. 2. A college or university considered to be provincial and unsophisticated.

cow (kou'ar) *intr.v.* **-ered**, **-er-ing**, **-ers**. To cringe in fear. [Middle English *cowen*, of Scandinavian origin.]

cowes (kouz). A town on the northern coast of the Isle of Wight in southern England. It is the headquarters of the Royal Yacht Squadron and the site of annual fashionable regattas. Population,

1. An effort to keep small whales, porpoises, or similar aquatic mammals, especially a whale of the genus *Mesoplodon*, having a pointed snout, from various marine fishes of the family Ostraciidae, especially *Acropora quadricornis* of warm Atlantic waters, having spines over each eye.

cowled (kōuld) *adj.* 1. Wearing or supplied with a cowl; hooded. 2. Having the shape of a hood.

Cowley (kou'lē), *Abraham*. 1618–1667. English metaphysical poet whose works include *David's* (1658), an epic on the life of King David.

Cowley, *Makolm*. 1898–1989. American writer, editor, and critic whose works include studies of American expatriate writers of the 1920's and commentaries on William Faulkner.

cow-lick (kou'lik') *n.* A projecting tuft of hair on the head that grows in a different direction from the rest of the hair and will not lie flat.

cowling (kou'ling) *n.* A removable metal covering for an engine, especially an aircraft engine.

cowman (kou'man, -mān') *n.* 1. An owner of cattle or a cattle ranch. 2. *a.* See *cowboy* (sense 1). *b.* A cowherd.

co-work-er or **co-work-er** (kō'wŭr'kər) *n.* One that works with another; a fellow worker.

cow parsnip *n.* Any of several tall, coarse herbs of the genus *Heracleum* in the parsley family, native chiefly to northern temperate regions and having compound umbels of small flowers.

cow-pea (kou'pē') *n.* 1. An annual African plant (*Vigna unguiculata*) in the pea family, widely cultivated in warm regions for food, forage, and soil improvement. 2. An edible seed of this plant. Also called *black-eyed pea*, *catjang*.

Cowper (kō'pər, kou'pər, kōp'ər), *William*. 1731–1800. British poet considered a precursor of romanticism. His best-known work, *The Task* (1785), praises rural life and leisure.

Cowper's gland (kou'pərz, kōp'-) *n.* See *bulbourethral gland*. [After William Cowper (1666–1709), English surgeon.]

cow pilot *n.* See *sergeant major* (sense 3).

cow-poke (kou'pōk') *n.* See *cowboy* (sense 1).

cow pony *n.* A small, agile horse used in herding cattle.

cow-pox (kou'pōks') *n.* A mild, contagious skin disease of cattle, usually affecting the udder, that is caused by a virus and characterized by the eruption of a pustular rash. When the virus is transmitted to humans, as by vaccination, it can confer immunity to smallpox. Also called *vaccinia*.

cow-punch-er (kou'pān'cher) *n.* See *cowboy* (sense 1).

cow-rie or **cow-ry** (kou'rē) *n.*, *pl.* *-ries*. Any of various tropical marine gastropods of the family Cypræidae, having glossy, often brightly marked shells, some of which are used as currency in the South Pacific and Africa. [Hindi *kaurī*, from Sanskrit *kapardikā*, diminutive of *kapardak*, shell, of Dravidian origin.]

co-write (kō'rit') *tr.v.* **-wrote** (-rōt'), **-writ-ton** (-rit'n), **-writ-ing**, **-writes**. To write jointly or in collaboration with another author. — **co-writ-er** *n.*

cow-ry (kou'rē) *n.* Variant of *cowrie*.

cow shark *n.* Any of several sharks of the family Hexanchidae of warm and temperate seas.

cow-shed (kou'shed') *n.* A shed for housing cows.

cow-slip (kou'slip') *n.* 1. A Eurasian primrose (*Primula veris*), usually having fragrant yellow flowers, widely cultivated as an ornamental, and long used in herbal medicine. 2. See *marsh marigold*. 3. The Virginia cowslip. [Middle English *cowslippe*, from Old English *cowslippe*: *cū*, cow; see *g^ou-* in Appendix + *slippa*, slime; see *slough-* in Appendix.]

cow town *n.* A small town in a cattle-raising area.

COX (kōks) *Nautical. n.* A coxswain. — **cox** *intr. & tr.v.* **coxed**, **cox-ing**, **cox-es**. To act as coxswain or serve as coxswain for.

COX-A (kōk'sə) *n.*, *pl.* **COX-AE** (kōk'sē'). 1. *Anatomy*. The hip or hip joint. 2. *Zoology*. The first segment of the leg of an insect or other arthropod, joining the leg to the body. [Latin, *hip*.] — **cox'al** *adj.*

COX-AL-GI-A (kōk-sāl-jē-ə, -jə) *n.* Pain in or disease of the hip or hip joint. [COX(A) + -ALGIA.] — **cox-al-gic** (-jik) *adj.*

cox-comb (kōks'kōm') *n.* 1. A conceited dandy; a fop. 2. *Obsolete*. A jester's cap; a cockscomb. [Middle English *cokkes comb*, crest of a cock: *cokkes*, genitive of *cock*, cock; see *COCK* + *comb*, crest; see *COCK*.]

cox-comb-er (kōks'kōm'rē, -skām-) *n.*, *pl.* *-ries*. Behavior that is characterized by an attitude of superiority to a coxcomb; fanciful con-



cow



cowrie

coxswain
Coxswain and rower